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Transplantation in mesangiocapillary glomerulonephritis with intramembranous dense "deposits": Recurrence of disease

DAVID R. TURNER, J. STEWART CAMERON, MICHAEL BEWICK, PAUL SHARPSTONE, DAVID MELCHER, CHISHOLM S. OGG, DAVID J. EVANS, ANTHONY J.P. TRAFFORD AND SIDNEY LEIBOWITZ

Departments of Medicine and Pathology, Guy's Hospital, London; Department of Morbid Anatomy, Royal Postgraduate Medical School, London; and Renal Unit and Department of Pathology, Royal Sussex County Hospital, Brighton, Sussex, England

Transplantation in mesangiocapillary glomerulonephritis with intramembranous dense "deposits": Recurrence of disease. Six patients with mesangiocapillary glomerulonephritis and intramembranous dense "deposits" developed terminal renal failure and were transplanted, three from living and three from cadaver donors. Eight renal biopsy specimens were obtained from five of the grafts, from 1 to 26 months following transplantation. All six biopsy specimens taken later than seven months following the graft showed recurrence of dense intramembranous "deposits" in the basement membranes of glomeruli, and of Bowman's capsule and tubular basement membrane in five. Recurrence of "deposits" was associated with deposition of C3 on immunofluorescent study in all but one specimen; in addition, IgM was found in two specimens, but IgG and early complement components were absent. Only two patients, however, showed glomerular proliferation associated with profuse proteinuria. In the other subjects the recurrence of the "deposit" was not associated with clinical findings. Graft loss, which occurred in two patients, was predominantly from rejection.

Transplantation dans la glomerulopathie à dépôts denses intramembraneux: Récidive de la maladie. Six malades atteints de glomérulopathie à dépôts denses intra-membraneux ont atteint le stade d'insuffisance rénale terminale et ont été transplantés. Trois d'entre eux ont reçu un rein de donneur vivant et les trois autres un rein de cadavre. Huit biopsies rénales ont été réalisées sur cinq de ces transplants un à trente-six mois après la transplantation. Les six biopsies prélevées après le septième mois de la transplantation montrent toutes la récidive des dépôts denses intra-membraneux dans les glomérules et cinq d'entre elles montrent aussi ces dépôts dans la capsule de Bowman et la membrane basale tubulaire. La récidive des dépôts est associée à la présence de C3, révélée par l'étude en immunofluorescence, dans toutes les biopsies sauf une. De plus, de l'IgM a été trouvée dans deux biopsies mais l'IgG et les facteurs précoces du complément sont absents. Deux malades seulement ont une prolifération glomérulaire associée à une protéinurie importante. Chez les autres, la récidive des dépôts n'est pas contemporaine de manifestations cliniques. La destruction du greffon, qui est survenue chez deux malades, a été essentiellement le fait du rejet.

Galle [1] and Berger, Galle and Ganter [2,3] drew attention to a striking glomerular lesion associated with some patients with proliferative glomerulonephritis. On electron microscopy, they found extensive, ribbon-like amorphous electron-dense osmiophilic material within the basement membranes throughout the kidney, affecting not only the glomeruli but also Bowman's capsule, tubules and peritubular capillaries on occasion. They also described the tinctorial properties of this material on optical microscopy: it takes many stains with avidity, but rejects silver impregnation [3]. Diagnosis is thus possible on optical microscopy of paraffin-embedded material [4] or, better, of 1 μm plastic-embedded sections [7].

The finding of this intramembranous material is usually associated with a glomerulonephritis classified upon optical microscopy as mesangiocapillary (also called membranoproliferative, parietoproliferative and, in some cases, lobular glomerulonephritis) [4-9]. About 20 to 30% of patients classified in this way show such intramembranous lesions [4-9], the remainder having some variety of subendothelial deposit [4-9]. The patients with intramembranous dense "deposits" usually present with a nephrotic syndrome, sometimes with an initial acute nephrotic episode [4-10] and evolve into chronic renal failure, half having died of uremia within eight to ten years [4-9, 11]. We have confirmed the presence of intramembranous dense deposits in 19 patients with mesangiocapillary glomerulonephritis (MCGN) [8]. Nine of these patients have developed terminal renal failure, and in six renal transplantation was performed. This paper gives details of the clinical evolution and the findings upon renal biopsy of the grafts; details of the complement findings are being prepared for publication elsewhere (Williams DG, Cameron JS, Peters DK).

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Methods

A. Renal biopsies. The patient's own kidney was biopsied using a Franklin-modified Vim-Silverman needle in the prone position. The two biopsy specimens taken before 1968 were fixed in buffered formalin alone. Subsequent biopsy specimens were fixed in Bouin (Dubosq-Brazil) and postfixed in formalin. All specimens were embedded in paraffin and cut at 3 μm for optical microscopy. In the case of patients 4, 5 and 6 (Tables 1 and 2), and during nephrectomies on patients 1 and 6; 1 mm cubes were also immersed in paraformaldehyde buffered with cacodylic acid-cacodylate buffer, postfixed in osmium tetroxide, embedded in araldite and cut at 1 μm for optical microscopy and 50 nm for electron microscopy. Material from patients 4, 5 ands 6 was also snapfrozen for immunofluorescent study.

The allograft kidneys were biopsied using a Vim-Silverman needle on eight occasions in five patients (Table 2). In one instance (patient 3) the biopsy specimen was taken during an exploration of the kidney. All these specimens were processed as above for optical, electron and immunofluorescence studies. Three transplants were removed from two patients, but only paraffin-embedded material was studied. For immunofluorescent study antisera were used directed against C1q, C3, C4, IgA, IgM, IgG and fibrinogen, and the preparations were viewed using a microscope (Leitz Orthoplan) with an interference filter (K500 FITC) and red suppression (BC38) and barrier filters (K510).

B. Clinical studies. Details of the patients' courses are given in Table 1 and in the histories (see Appendix). Patient 6 did not have a renal biopsy of his allograft. C3 complement measurements were made by radial immunodiffusion using either commercially available goat anti-human C3 antiserum (Hyland Laboratories) or a locally produced monospecific anti-human C3 antiserum raised in sheep. The range of values found in sera from normal subjects varied from 60 to 160% of a reference pooled normal serum.

Results

Initial biopsies of patient's own kidney. All biopsy specimens showed dense, intramembranous ribbon-like material in the basement membranes throughout the specimen, most prominently in the glomeruli (Fig. 1). In all patients there was increased cellularity of the glomeruli and an enlarged glomerulus with an increased lobularity [9]. In the case of patient 5, the immunofluorescent study showed strong C3, together with weak Clq, IgA and IgM on the glomerular basement membranes; properdin was also present in the mesangium. Patient 6's nephrectomy showed only occasional glomerular deposits of C3. In patient 4, no immunofluorescence was demonstrated.

Transplant biopsies. Five patients were biopsied eight times from 1 to 26 months following transplantation. The results on optical electron and immunofluorescent microscopy are summarised in Table 2. All five patients biopsied showed evident recurrence of the intramembranous, electron-dense deposit-like material similar to that seen by electron microscopy of three of the original specimens of the patients' own kidneys, and on optical microscopy in the other three.

1. Electron microscopy. Illustrative pictures of the lesions are shown in Figs. 2-5. The initial biopsy specimen in patient 1 showed, besides the evidence of a minor deposit within the basement membrane, obvious glomerular proliferation and cellular infiltration, together with subepithelial "humps" on electron microscopy. This patient had received a course of horse anti-lymphocyte globulin (ALG), to which he reacted, and it is possible that this represents a reaction to the ALG and not a feature of the recur-

Table 1. Clinical details[a]

Patient No.	Sex	Age at transplant	Duration of known disease	Presentation	Source of graft	Graft failure	Present status	Remarks
1	m	19 yr	6 yr	AGN→NS	1) CD 2) CD	Yes Yes	Regular dialysis	
2	m	19 yr	5 yr 8 mo	PP	CD	—	Functioning graft	
3	m	20 yr	2 yr 4 mo	NS	LD (mother)	Yes	Dead	Partial lipodystrophy
4	m	10 yr 6 mo	9 mo	NS	LD (father)	—	Functioning graft	
5	m	22 yr	2 yr	NS→CRF	CD	—	Functioning graft	Partial lipodystrophy
6	m	19 yr	5 yr 4 mo	CRF	LD (father)	—	Functioning graft	

[a]m, male; NS, nephrotic syndrome; PP, persistent proteinuria; AGN, acute glomerulonephritis; CRF, chronic renal failure; CD, cadaver graft; LD, live donor graft.

Table 2. Histologic findings in transplant biopsy specimens[a]

Patient No.	Time of biopsy after transplant *months*	Electron microscopy findings			Optical microscopy findings				Immunofluorescent findings					
		Deposits in glomerular capillary loops	Deposits in Bowman's capsule	Deposits in tubular basement membrane	Mesangial cell prolif.	Mesangial cell inter-position	Evidence of rejection	C3 in glomeruli	C3 in tubules/ Bowman's capsule	Clq	C4	IgM	IgG	IgA	Fibrinogen
1 (1)	4	Large subepithelial ++ Small subendothelial +	–	–	+	–	±	+	+	nd	nd	+	+ (linear, faint)	–	occ
(2)	8	Linear dense deposit +++	++	++	+	+	++	+	–	–	nd	–	+	–	–
2	7	Linear dense deposit + Mesangial ++ Subendothelial +	–	±	+	–	–	+	+	–	nd	–	–	–	occ
3	12	Linear dense deposit +++	++	++	++	+	++	+	+	–	nd	–	–	–	occ
4 (1)	12	Linear dense deposit +++	++	++	+++	+++	–	+	+	–	–	–	–	–	–
(2)	28	Linear dense deposit ++	++	+	++	+	+	nd	nd	nd	nd	nd	nd	nd	nd
5 (1)	1	Mesangial ++ Subepithelial +	±	–	+	–	+	±	+	–	–	–	–	–	–
(2)	13	Linear dense deposit ++	++	++	+	–	++	–	–	–	–	–	–	–	occ

[a]No posttransplant biopsy was performed on patient 6. nd, not done; occ, occasional.

rent nephritis. However, occasional "humps" have been noted in some specimens from patients with intramembranous deposits [6,9]. "Humps" were absent from the second biopsy specimen, taken four months later (Fig. 2) which showed obvious intramembranous lesions. Similar good evidence of recurrence of the material was obtained in patients 3, 4 and 5, although in the latter patient no intramembranous material was seen in the initial biopsy specimen, taken during an acute urinary tract infection only four weeks after the graft. In the specimen taken at 13 months following graft, however, the lesions were present.

2. Optical microscopy. In contrast to the regular appearance of the intramembranous material in these grafted kidneys, the appearances on optical microscopy were more variable. The acute proliferative lesion present in the first biopsy specimen of patient 1 has already been mentioned. All specimens showed to some extent lesions attributable to chronic rejection, which makes interpretation of any supposedly nephritic lesions more difficult. However, patients 3 and 4 showed obvious mesangial expansion and proliferation, and patient 5 showed the same in his second biopsy specimen, but to a lesser degree. The other three specimens showed no changes which could be described as nephritis.

3. Immunofluorescent studies. The immunofluorescent findings are summarized in Table 2 and illustrated in Figs. 6-8. Deposits of C3 were found in the glomeruli (Fig. 6), usually in the parietal part of the glomerulus rather than the mesangium. In addition, four patients showed strong fluorescence with anti-C-3 antiserum in the tubular basement membrane (Fig. 7) and in Bowman's capsule. In the first biopsy specimen of patient 5, evidence of an acute infection was present and so the finding of C3 in Bowman's capsule and in tubules must be interpreted cautiously. IgM was present in two specimens (Fig. 8) and faint, linear IgG was seen throughout the basement membranes in glomeruli of two specimens. IgA was never seen. Flecks of fibrin were occasionally seen, but were never prominent.

Clinical data: Table 1 and the histories in the Appendix give details. Three patients (1, 3 and 4) developed profuse proteinuria, in two cases (patients 3 and 4) leading to a full nephrotic syndrome and edema. In the case of patient 4, this remitted and then reappeared 14 months later. Rebiopsy showed a definite nephritis in both of patient 4's specimens, worse on the second occasion (Table 2). In patients 1 and 3, the graft was failing from chronic rejection and was lost in both patients from this cause. However, patient 3 showed definite proliferative glomerulonephritis in

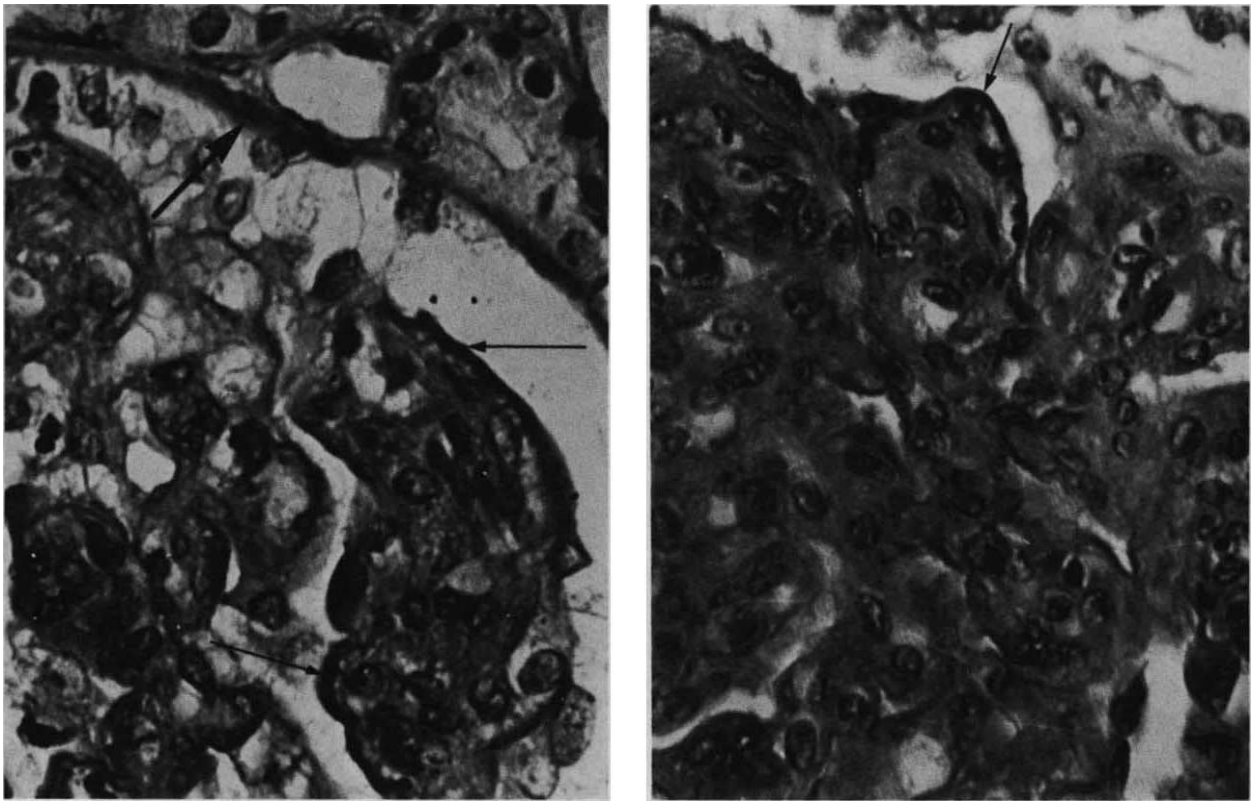

Fig. 1. *Photomicrograph of parts of two glomeruli from patient 3, showing dense "deposit" in capillary basement membrane* (small arrows) *and in Bowman's capsule basement membrane* (large arrow) *(PAS stain, ×500).*

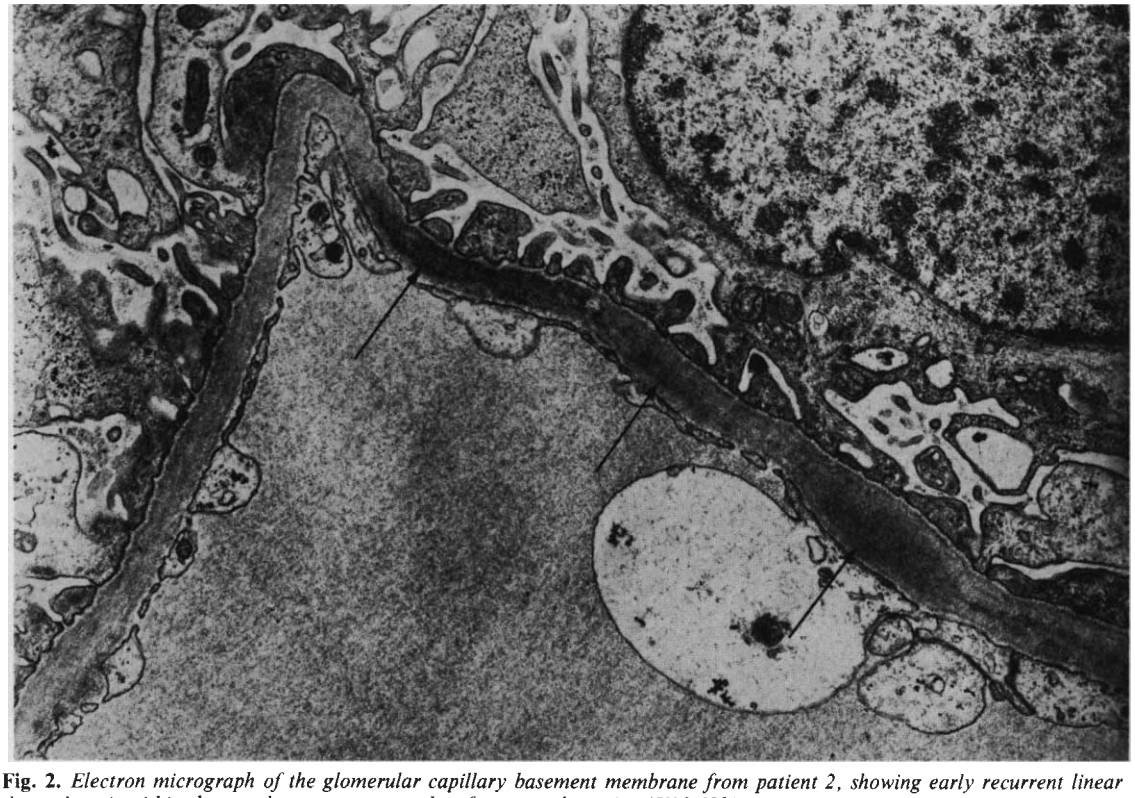

Fig. 2. *Electron micrograph of the glomerular capillary basement membrane from patient 2, showing early recurrent linear dense deposit within the membrane, seven months after transplantation (X10,600).*

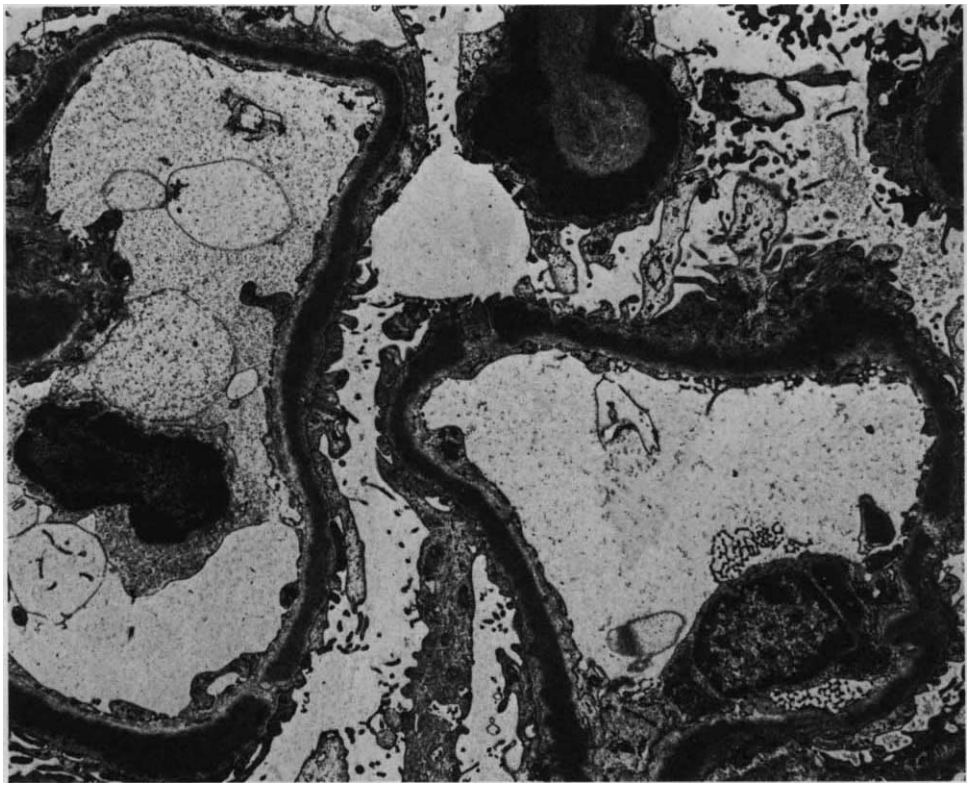

Fig. 3. *Electron micrograph of two full capillary loops (patient 1, second biopsy) showing almost continuous linear dense deposit within the membrane, eight months after transplantation (X6,000).*

Fig. 4. *Electron micrograph of a capillary loop (patient 3) filled with proliferating mesangial cell processes (X8,000).* The capillary basement membrane contains intermittent linear dense deposits, 12 months after transplantation.

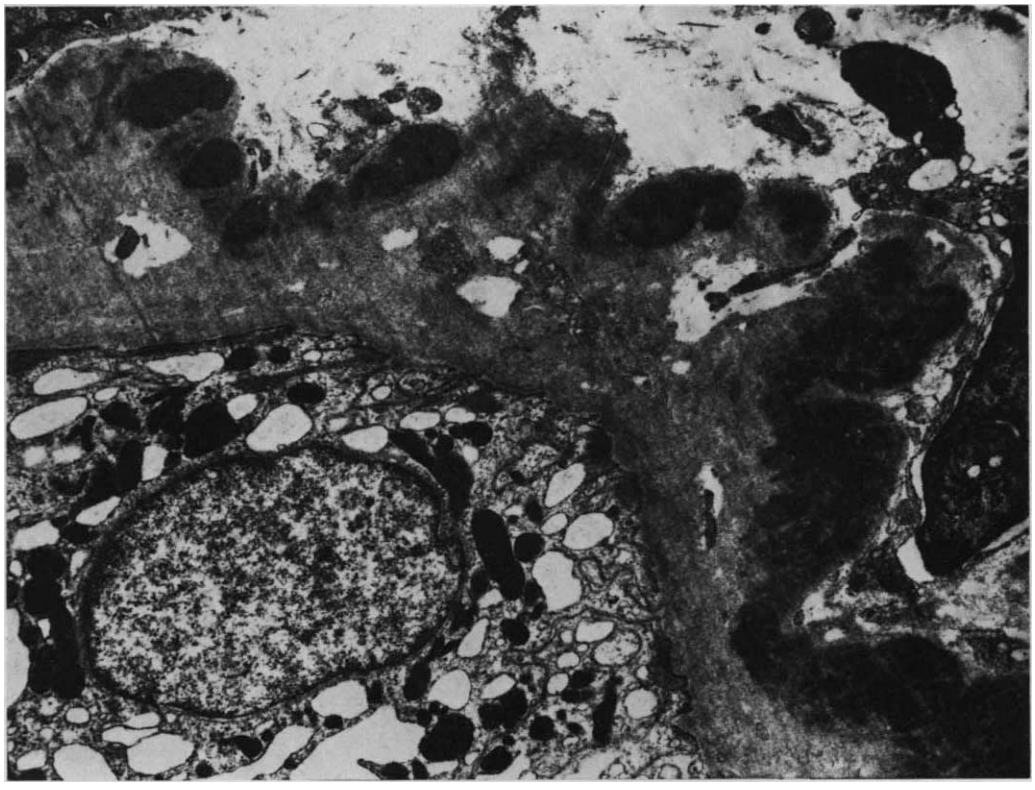

Fig. 5. *Electron micrograph of the basement membrane of a proximal renal tubule (patient 5) showing intermittent linear dense deposit, seven months after transplantation (X8,000).*

the biopsy specimen taken late in the course of the graft. Patient 6, who has yet to have a biopsy, remains well without proteinuria.

Serial C3 serum concentrations in all six patients before and after grafting are illustrated in Fig. 9. Details of full complement profiles and C3NeF activity are being prepared for publication (Williams DG, Cameron JS, Peters DK). All patients showed low (<35% normal) C3 concentrations before grafting; immediately after the operation, this rose to low normal levels in patients 2, 5 and 6, and more slowly in patient 1. In patient 4 and especially in patient 3 it remained low.

Discussion

In 1971, Galle, Hinglais and Crosnier [12] presented preliminary electron microscopic evidence that the intramembranous dense "deposits" could

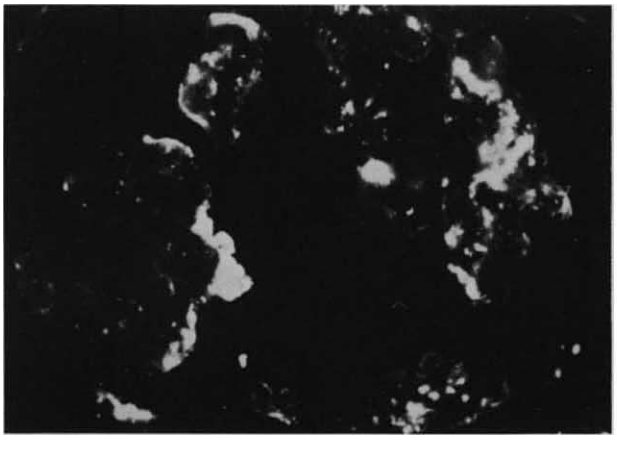

Fig. 6. *Immunofluorescent study using anti-C3 antiserum (patient 3) 12 months after transplantation.* There are extensive deposits of C3 within the glomeruli.

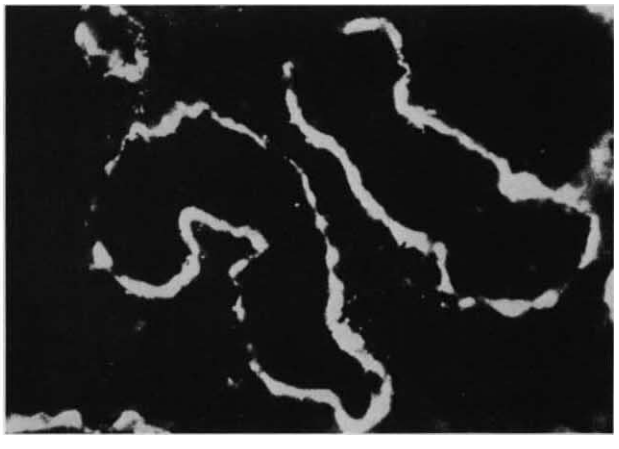

Fig. 7. *Immunofluorescent study using anti-C3 antiserum (patient 1).* The tubular basement membranes show strong immunofluorescence.

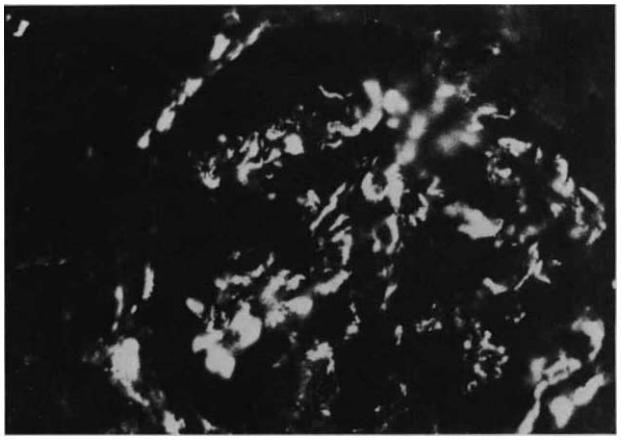

Fig. 8. *Immunofluorescent study using anti-IgM antiserum (patient 1).* There are extensive deposits of IgM within the glomeruli and in Bowman's capsule.

recur in transplanted kidneys. More recently, Galle and Mahieu have presented some further data on this subject [8].

Our data confirm and extend their conclusions, and suggest that in view of the relatively small number of patients studied, transmission to the grafted kidney is a frequent and perhaps invariable event. The appearance of the deposits in the grafted kidney is also swift, as in Galle's patients; during the first year, no deposits were visible at 1 month, slight deposits were seen at 4 and 7 months, while the remaining specimens biopsied from 8 to 26 months all showed obvious lesions. Dense intramembranous material was not observed in any of more than 150 specimens from transplants in patients with other forms of nephritis.

In three of the patients from Paris and one of ours, there were no clinical signs whatsoever of the presence of the deposits in the kidney; in three of our patients proteinuria and microscopic hematuria only were present, and only two patients developed profuse proteinuria and the nephrotic syndrome, which cleared in one after a few weeks, only to recur 14 months later. Within the time scale of observation and within the circumstances of transplantation (which includes immunosuppression), the reappearance of dense "deposits" is only accompanied either by histological or clinical evidence of glomerulonephritis in a minority of patients.

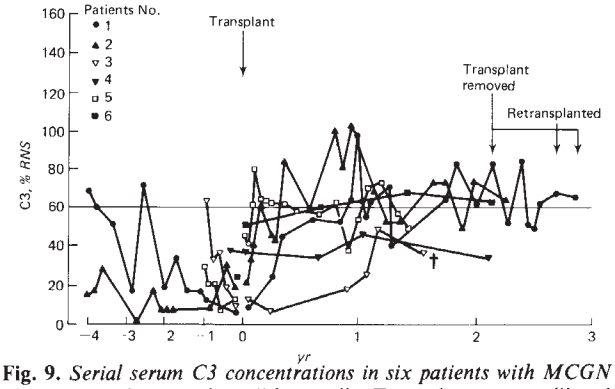

Fig. 9. *Serial serum C3 concentrations in six patients with MCGN and intramembranous dense "deposits".* "Transplant removed" and "retransplanted" refer to patient 1. + = death; RNS = reference normal serum.

The appearance of the material within the basement membranes throughout the kidney clearly depends upon some humoral factor(s) which persists following transplantation. We have shown that not only does material visible on electron microscopy appear, but that both glomerular and other basement membranes may contain C3 demonstrable by immunofluorescent techniques. In the glomeruli of two patients, IgM was visible. Some transplant biopsy specimens may show weak C3 or IgM fluorescence, especially in the presence of chronic rejection, but in our experience not of the intensity of distribution seen in these patients, and above all not so early following transplantation.

Although referred to as "deposits" since their first description, there is as yet no evidence that this material represents deposit of circulating substances, particularly circulating antibody-antigen complexes. The appearance of C3 in the absence of immunoglobulin and classical C components (C1, C4 and C2) suggests that the origin of the disease is different from the usual soluble complex diseases, although it does not exclude the possibility. Immunoglobulin may be present but masked by C3; and C3, once fixed, persists much longer than immunoglobulin in both clinical and experimental renal diseases [13, 14]. If the material is the result of soluble antigen-antibody complex deposition, then these complexes must be of a nature and size to explain their intramembranous situation. The finding of IgM in some patients [9], and in some grafted kidneys, may be of significance, although in animal systems IgM complexes usually do not localize in the glomerular capillary wall [15]. However, mixed IgG-IgM cryoglobulins may deposit in a granular fashion in the capillary wall [16].

An alternative explanation is to regard the glomerular and other basement membrane changes as transformations of the chemical substance of the basement membrane [8]. If so, this must depend upon a humoral factor. Any theory explaining the nature of dense "deposit" disease must, in addition, account for the association with alternate pathway complement activation on the one hand, and in some patients with partial lipodystrophy, as in two of the

patients reported here. Peters and Williams [17] have presented evidence for the priority of the complement changes. In our patients, the reappearance of the original lesions occurred in the patients whose C3 concentration returned to normal after transplantation (patients 1, 2 and 6) and in those in whom it remained low (patients 3 and 4) although it is true that nephritis and a nephrotic syndrome were observed in addition in patients 3 and 4.

Should patients with this form of nephritis and intramembranous dense "deposits" be transplanted, in view of the recurrence of the material in the basement membranes of the allograft? In only two of the six patients reported here, and in none of the patients of Galle et al [8, 12] was there obvious glomerulonephritis, although three of our patients had developed profuse proteinuria and two a nephrotic syndrome (see Appendix). The two graft failures were the result of rejection, not the recurrent glomerulonephritis. However, the period of observation is still very short, and if the results of transplantation improve, then recurrent nephritis of all types is almost certain to assume greater importance as a cause of graft failure. Cadaver transplantation in these patients is probably justified, but the increased risk to the allograft makes live organ donation a less attractive prospect. In addition, the donation of organs in what may be, in some or all instances, an inherited complement abnormality, could have unknown effects on the graft. Intrafamilial transplants in this situation should, therefore, be viewed with caution.

Appendix: Case histories

Patient 1. This man presented with an acute nephritic illness following an upper respiratory tract infection in August, 1966. Proteinuria persisted with microscopic hematuria and a nephrotic syndrome appeared. Biopsy in October, 1966 showed mesangiocapillary glomerulonephritis with some crescents. The C3 concentration was 33 mg/100 ml. He was treated for three months with cyclophosphamide, and the C3 value became normal briefly. During this time his creatinine concentration rose from 40 to 115 ml/min. Over the next three years he maintained a variable proteinuria, edema and microscopic hematuria, but during 1969 his renal function declined rapidly despite control of hypertension. Three months' treatment with azathioprine, 150 mg, and prednisone, 20 mg/day, was given without effect. Dialysis was begun in July, 1970 and after a period of home dialysis he was given a two-mismatch cadaver graft on March 21, 1972. Graft function never reached entirely normal levels and hypertension was a constant problem. Because of this a bilateral nephrectomy was performed in February, 1973. During this period, plasma creatinine concentration averaged 2.5 mg/100 ml and proteinuria varied from 2.5 to 7.7 g/day with intermittent microscopic hematuria. Following control of blood pressure proteinuria fell to 0.5 to 1.8 g/day. In March, 1974 graft function declined rapidly and on this occasion antirejection treatment failed to control the decline. He was restarted on hemodialysis on May 4, 1974 and the transplant was removed shortly thereafter. After a period on regular hemodialysis he was retransplanted on June 26, 1974, but the graft was removed two months later. He is currently receiving maintenance hemodialysis.

Patient 2. This orphan was found on routine urine testing to have proteinuria and microscopic hematuria in October, 1967. Renal biopsy in January, 1968 showed MCGN and his C3 was extremely low, varying from undetectable to 15 mg/100 ml. Renal function remained normal until May, 1969, but by May, 1970 when next seen glomerular filtration rate (GFR) had fallen to 42 ml/min. At this time he had an episode of acute pneumococcal peritonitis. In May, 1971 his GFR was only 11 ml/min, and he had severe hypertension requiring drug treatment; in February, 1973 his GFR had fallen to 7 ml/min. He was transplanted without preliminary dialysis with a three-antigen cadaver donor kidney with one known mismatch. His own kidneys were removed at the same operation. Biopsy of the graft was done on September 7, 1973. He now has a plasma creatinine concentration of 1.5 mg/100 ml, a creatinine clearance of 65 ml/min and trace to 0.8 g/day of proteinuria.

Patient 3. This man presented with a nephrotic syndrome in September, 1968. A renal biopsy in December, 1968 showed MCGN and his plasma C3 was 22 mg/100 ml. He was treated with cyclophosphamide for six months without success, his nephrotic syndrome persisting, and his GFR fell from 33 to 5 ml/min in July, 1969, when hemodialysis was begun. A bilateral nephrectomy was done in December, 1969, and he was later transplanted with a two-mismatch kidney from his mother on January 13, 1970. The graft initially functioned well, a plasma creatinine concentration of 1.4 mg/100 ml and a creatinine clearance of 120 ml/min being recorded in May, 1970. Function declined over the next six months, however, and biopsy in July, 1971 showed clear evidence of recurrent dense intramembranous material with some glomerular proliferation. Proteinuria was less than 1.0 g/day until April, 1971 (at which time the creatinine clearance

was still above 100 ml/min) when it rose to 2 to 4.5 g/day. Peak proteinuria was 7.7 g/day at a clearance of 28 ml/min in July, 1971. Peritoneal dialysis was started on August 30, 1971 because of renal failure, but he died on September 15, 1971 of infection. In retrospect his appearance was thought to be typical of partial lipodystrophy, and this was confirmed by clinical photographs; no skin biopsy was performed, however.

Patient 4: This boy developed a sudden onset of the nephrotic syndrome at the age of 9 yr 11 mo. At this time he was mildly hypertensive (140/85 mm Hg) and had a reduced creatinine clearance (30 ml/min uncorrected for size) and a low plasma C3 concentration (50 mg/100 ml). A renal biopsy showed MCGN with intramembranous dense deposits and numerous crescents. Only three months later he required peritoneal dialysis despite attempts to control his hypertension, which became severe. After a brief period of hemodialysis, he received a two-mismatch kidney from his mother. Because of uncontrolled blood pressure, a bilateral nephrectomy was performed a week later. Graft function was immediate and eight months later he had a creatinine clearance of 83 ml/min, a serum creatinine concentration of 1.0 mg/100 ml and normal blood pressure. At this stage, however, microscopic hematuria and increasing proteinuria was noted. One year after receiving the graft he had macroscopic hematuria and profuse proteinuria (9.6 g/24 hr); there was some deterioration in graft function (serum creatinine concentration, 1.5 mg/100 ml; creatinine clearance, 45 ml/min) and a biopsy was performed. He was treated as if for rejection with i.v. administration of methylprednisolone, and there was rapid improvement. Within three months function, proteinuria and hematuria were all normal with a serum creatinine concentration of 1.0 mg/100 ml; creatinine clearance, 73 ml/min; urinary protein excretion, 0.4 g/24 hr; and no hematuria. He remained well with blood pressure 110/70 mm Hg, but with 0.9 to 1.7 g/24 hr proteinuria and a plasma creatinine concentration of 1.0 mg/100 ml; but 26 months after transplantation proteinuria increased again to a maximum of 21.5 g/24 hr, with a rise in serum creatinine to 3.6 mg/100 ml. A further biopsy was performed, and prednisone increased again to 100 mg/day. He was also heparinized, but this was stopped because of retroperitoneal bleeding. Now his proteinuria is 4.4 g/day, and his plasma creatinine concentration, 2.1 mg/day; he is being maintained on prednisone therapy, 50 mg/day.

Patient 5: This man developed a nephrotic syndrome in November, 1971 with normal renal function (creatinine clearance, 133 ml/min). Only one year later, in November, 1972, he was fully investigated. A renal biopsy specimen showed MCGN with intramembranous dense deposits and examination of the patient showed the facies of partial lipodystrophy. A biopsy specimen of the upper half of the body showed the absence of subcutaneous fat. His C3 was 20% of normal. He still had a very low serum albumin concentration (1.7 g/100 ml) but his plasma creatinine value was 22 mg/100 ml, and peritoneal dialysis was begun. Later, hemodialysis was continued and on December 8, 1973 he received a one-mismatch cadaver kidney with passive enhancement of the HL-A mismatch. This kidney functioned immediately but major problems were encountered with a urinary leak from a cystotomy closure and recurrent urinary tract infections. During an episode of acute infection, a renal biopsy was performed on December 14, 1973 because of the possibility of coincident rejection. This biopsy showed acute pyelonephritis. Graft function was good and in May, 1974, plasma creatinine concentration was 1.3 mg/100 ml, and creatinine clearance, 73 ml/min; only trace proteinuria was present. Current proteinuria is 0.3 g/24 hr. A second renal biopsy was done on December 15, 1974 because of a rising plasma creatinine concentration (1.9 to 2.1 mg/100 ml). He remains well with a plasma creatinine value of 2.0 mg/100 ml.

Patient 6: In 1968 this man was noted to be hypertensive, but no other observations were recorded. From July, 1972, he became progressively more tired, and in January, 1973 his blood urea concentration was found to be 270 mg/100 ml, and his diastolic blood pressure, 130 mm Hg. A renal biopsy (Dr. A. M. Joekes) showed MCGN with intramembranous deposits and his C3 was 35 mg/100 ml. Hemodialysis was begun and on April 18, 1973 he received a two-mismatch kidney from his father. Graft function is good, he has returned to his home in Cyprus and in May, 1974 his blood urea concentration was 28 mg/100 ml with only a trace of proteinuria. No biopsy of this graft has yet been performed, but bilateral nephrectomy was done in June, 1975 for severe hypertension. At this time blood urea concentration was 100 mg/100 ml, and plasma creatinine, 1.4 mg/100 ml.

Acknowledgments

Dr. A. M. Joekes and Dr. R. Pugh supplied material from the original biopsy of patient 6, and Mr. F. G. Ellis granted permission for us to study the patient. Bob Francis and Rodney Machling processed the biopsy material, and Barry Nester produced the electron micrographs.

Reprint requests to Dr. J. S. Cameron, Department of Medicine, Guy's Hospital Medical School, London, SE1 9RT, United Kingdom.

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